CLAIMS

1. An endogenous repair factor production accelerator, which comprises one or at least two selected from a PGI2 agonist, an EP2 agonist and an EP4 agonist.

2. The endogenous repair factor production accelerator according to claim 1, wherein the endogenous repair factor is a vascular endothelial growth factor, a hepatocyte growth factor, a fibroblast growth factor, a transformation growth factor-β, a platelet derived growth factor, a bone morphogenetic protein or an epidermal growth factor.

3. The endogenous repair factor production accelerator according to claim 1, which is a stem cell differentiation inducer.

4. The endogenous repair factor production accelerator according to claim 1, which is an angiogenesis accelerator.

5. The endogenous repair factor production accelerator according to claim 1, which is a persistent prerparation which further comprises a biodegradable polymer.

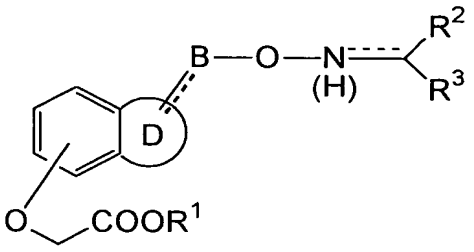
6. The endogenous repair factor production accelerator according to claim 5, wherein the persistent preparation is a microsphere preparation, a microcapsule preparation or a nanosphere preparation.

7. The endogenous repair factor production accelerator according to claim 1, which is an agent for preventing and/or treating organ diseases.

8. The endogenous repair factor production accelerator according to claim 7, wherein the organ disease is an ischemic organ disease, a liver disease, a kidney disease, a lung disease, a pancreas disease, a bone disease, a digestive organ disease, a nerve degeneration disease, a diabetic complication, a vascular endothelial cell disease, a heart disease, a dental disease, decubitus, glaucoma or alopecia.

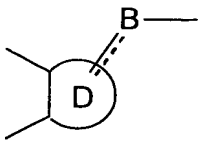
9. The endogenous repair factor production accelerator according to claim 8, wherein the ischemic organ disease is arteriosclerosis obliterans, Buerger disease, Raynaud disease, myocardial infarction, angina pectoris, diabetic neuropathy, spinal canal stenosis, cerebrovascular accidents, cerebral infarction, pulmonary hypertension, bone fracture or Alzheimer disease.

10. The endogenous repair factor production accelerator according to claim 1, wherein the PGI2 agonist is a compound represented by formula (I):

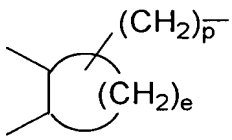


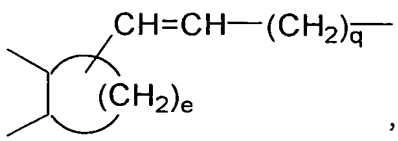
(I)

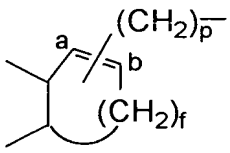
wherein

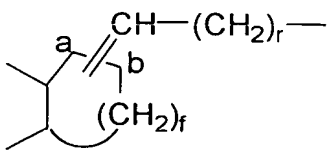


is

(i)  ,

(ii)  ,

(iii)  or

(iv) 

wherein R^1 represents hydrogen or C1-4 alkyl;

R^2 represents (i) hydrogen, (ii) C1-8 alkyl, (iii) phenyl or C4-7 cycloalkyl, (iv) a 4- to 7-membered monocyclic ring containing one nitrogen atom, (v) C1-4 alkyl substituted with a benzene ring or C4-7 cycloalkyl, or (vi) C1-4 alkyl substituted with a 4- to 7-membered monocyclic ring containing one nitrogen atom;

R^3 represents (i) C1-8 alkyl, (ii) phenyl or C4-7 cycloalkyl, (iii) a 4- to 7-membered monocyclic ring containing one nitrogen atom, (iv) C1-4 alkyl substituted with a benzene ring or C4-7 cycloalkyl, or (v) C1-4 alkyl substituted with a 4- to 7-membered monocyclic ring containing one nitrogen atom;

e represents an integer of from 3 to 5;

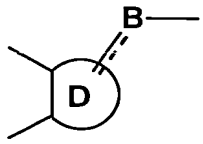
f represents an integer of from 1 to 3;

p represents an integer of from 1 to 4;

r represents an integer of from 1 to 3;

q represents an integer of 1 or 2, and

wherein, when



is the group represented by (iii) or (iv),

$-(CH_2)_p-$ and $=CH-(CH_2)_s-$ are bound to the position of a or b on the ring, and

the rings in R^2 and R^3 may be substituted with 1 to 3 of C1-4 alkyl, C1-4 alkoxy, halogen, nitro or trihalomethyl, or

a salt thereof.

11. The endogenous repair factor production accelerator according to claim 10, wherein the PGI2 agonist is

(1) (E)-[5-[2-[1-phenyl-1-(3-pyridyl)methylideneaminoxy]ethyl]-7,8-dihydronaphthalen-1-yloxy]acetic acid, or

(2) (Z)-[5-[2-[1-phenyl-1-(3-pyridyl)methylideneaminoxy]ethyl]-7,8-dihydronaphthalen-1-yloxy]acetic acid.

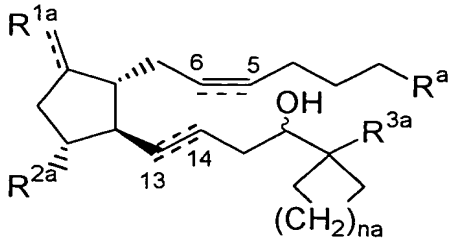
12. The endogenous repair factor production accelerator according to claim 1, wherein the PGI2 agonist is

(1) (±)-(1R,2R,3aS,8bS)-2,3,3a,8b-terahydro-2-hydroxy-1-[(E)-(3S,4RS)-3-hydroxy-4-methyl-1-octen-6-ynyl]-1H-cyclopenta[b]benzofuran-5-butanoic acid sodium salt,

(2) 5-{(3aR,4R,6aS)-5-hydroxy-4-[(1E,3S)-3-hydroxy-3-(cis-4-propylcyclohexyl)prop-1-enyl-3,3a,4,5,6,6a-hexahydrocyclopenta[b]pyrrol-2-yl}pentanoic acid methyl ester, or

(3) (5E)-5-[(3aS,4R,5R,6aS)-4-[(1E,3S)-3-cyclopentyl-3-hydroxyprop-1-enyl]-5-hydroxyhexahydropentalene-2(1H)-ylidene]pentanoic acid.

13. The endogenous repair factor production accelerator according to claim 1, wherein the EP2 agonist is a compound represented by formula (I-a):



(I-a)

wherein R^a represents carboxyl or hydroxymethyl;

R^{1a} represents oxo, methylene or halogen;

R^{2a} represents hydrogen, hydroxyl or C1-4 alkoxy;

R^{3a} represents hydrogen, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, or C1-8 alkyl, C2-8 alkenyl or C2-8 alkynyl substituted with 1 to 3 of the following groups (1) to (5): (1) halogen, (2) C1-4 alkoxy, (3) C3-7 cycloalkyl, (4) phenyl, (5) phenyl substituted with 1 to 3 halogen, C1-4 alkyl, C1-4 alkoxy, nitro or trifluoromethyl;

na represents 0 or an integer of from 1 to 4;

 represents a single bond or a double bond;

 represents a double bond or a triple bond; and

 represents a single bond, a double bond or a triple bond, and

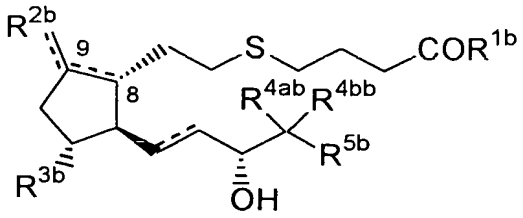
wherein (1) when the 5-6 position represents a triple bond, the 13-14 position does not represent a triple bond, and

(2) when the 13-14 position represents a double bond, the a double bond represents E form, Z form or EZ form,

a salt thereof, a prodrug thereof or a cyclodextrin clathrate thereof.

14. The endogenous repair factor production accelerator according to claim 13, wherein the EP2 agonist is (5Z,9β,11α,13E)-17,17-propano-11,16-dihydroxy-9-chloro-20-norprost-5,13-dienoic acid.

15. The endogenous repair factor production accelerator according to claim 1, wherein the EP4 agonist is a compound represented by formula (I-b):



(I-b)

wherein R^{1b} represents hydroxyl, C1-6 alkoxy or $-NR^{6b}R^{7b}$;

R^{6b} and R^{7b} each independently represents hydrogen or C1-4 alkyl;

R^{2b} represents oxo, halogen or $-O-COR^{8b}$;

R^{8b} represents C1-4 alkyl, phenyl or phenyl(C1-4 alkyl);

R^{3b} represents hydrogen or hydroxyl;

R^{4ab} and R^{4bb} each independently represents hydrogen or C1-4 alkyl;

R^{5b} represents phenyl substituted with a group of the following i) to iv):

i) 1 to 3 of

C1-4 alkoxy-C1-4 alkyl,

C2-4 alkenyloxy-C1-4 alkyl,

C2-4 alkynyloxy-C1-4 alkyl,

C3-7 cycloalkyloxy-C1-4 alkyl,

C3-7 cycloalkyl(C1-4 alkoxy)-C1-4 alkyl,

phenyloxy-C1-4 alkyl,

phenyl-C1-4 alkoxy-C1-4 alkyl,

C1-4 alkylthio-C1-4 alkyl,

C2-4 alkenylthio-C1-4 alkyl,

C2-4 alkynylthio-C1-4 alkyl,

C3-7 cycloalkylthio-C1-4 alkyl,

C3-7 cycloalkyl(C1-4 alkylthio)-C1-4 alkyl,

phenylthio-C1-4 alkyl, or

phenyl-C1-4 alkylthio-C1-4 alkyl,

ii) C1-4 alkoxy-C1-4 alkyl and C1-4 alkyl,

C1-4 alkoxy-C1-4 alkyl and C1-4 alkoxy,

C1-4 alkoxy-C1-4 alkyl and hydroxy,

C1-4 alkoxy-C1-4 alkyl and halogen,

C1-4 alkylthio-C1-4 alkyl and C1-4 alkyl,

C1-4 alkylthio-C1-4 alkyl and C1-4 alkoxy,

C1-4 alkylthio-C1-4 alkyl and hydroxy, or

C1-4 alkylthio-C1-4 alkyl and halogen,

iii) haloalkyl or hydroxy-C1-4 alkyl, or

iv) C1-4 alkyl and hydroxy; and

⁻⁻⁻⁻ represents a single bond or a double bond, and

wherein, when R^{2b} is -O-COR^{8b}, the 8-9 position represents a double bond,

a salt thereof or a cyclodextrin clathrate thereof.

16. The endogenous repair factor production accelerator according to claim 15, wherein the EP4 agonist is

(1) (11α,13E,15α)-9-oxo-11,15-dihydroxy-16-(3-methoxymethylphenyl)-17,18,19,20-tetranor-5-thiaprost-13-enoic acid, or

(2) (11α,13E,15α)-9-oxo-11,15-dihydroxy-16-(3-methoxymethylphenyl)-17,18,19,20-tetranor-5-thiaprost-13-enoic acid methyl ester.

17. A method for accelerating production of an endogenous repair factor in a mammal, which comprises administering to a mammal an effective amount of one or at least two selected from a PGI2 agonist, an EP2 agonist and an EP4 agonist.

18. A method for preventing and/or treating organ diseases in a mammal, which comprises administering to a mammal an effective amount of one or at least two selected from a PGI2 agonist, an EP2 agonist and an EP4 agonist.

19. Use of one or at least two selected from a PGI2 agonist, an EP2 agonist and an EP4 agonist for preparing an endogenous repair factor production accelerator.

20. Use of one or at least two selected from a PGI2 agonist, an EP2 agonist and an EP4 agonist for preparing an agent for preventing and/or treating organ diseases.

21. A pharmaceutical composition which comprises the endogenous repair factor production accelerator according to claim 1 in combination with one or at least two selected from an anti-thrombus agent, a circulation improving agent, a bronchial smooth muscle dilator, an anti-inflammatory drug, a local anesthetic, an analgesic, a bone cement, an joint lubricant, a PG derivative, an endogenous repair factor protein, an endogenous repair factor gene and a stem cell.